REMARKS

The final Office Action dated June 18, 2008 has been carefully reviewed and the following remarks are made in response thereto. In view of the following remarks, Applicants respectfully request reconsideration of this application and timely allowance of the pending claims.

Status of the Claims

Claims 83, 84, 87, and 88 are pending in the present application.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 83, 84, 87, and 88 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,113,907 to Khwaja et al. ("Khwaja et al.") in view of U.S. Patent No. 6,040,138 to Lockhart et al. ("Lockhart et al."). Specifically, the Examiner alleges that it would have been obvious to one skilled in the art to combine the gene array method of Lockhart et al. with the quality control method of Khwaja et al. to arrive at the present invention.

Applicants respectfully submit that the cited references do not render the claimed invention obvious because the combined disclosures of the cited references do not teach or suggest the claimed limitations of the present method. Furthermore, there is no disclosure or suggestion provided in the cited references, or otherwise of the record, which would motivate one skilled in the art to modify the methods of the cited references in such a way to arrive at the claimed invention.

Establishing *prima facie* obviousness requires a showing that the prior art references, when combined, teach or suggest all the claim limitations. Furthermore, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Recently, the United States Supreme Court also expressed the need to an "explicit" showing of "some apparent reason to combine the known elements in the fashion claimed by the patent at issue" and that "rejection on obviousness grounds cannot be sustained by mere

conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. __, 127 S.Ct. 1727, slip op. at 14 (2007).

The Examiner has questioned the meaning of "biosystem" used in the response filed on March 26, 2008. Applicants respectfully note that the term "biosystem" is specifically defined in the specification as "any biological entity for which biological responses may be observed or measured". Examples of a biosystem include cell, tissue, organ, whole organism, or *in vitro* assay. (See lines 26-28, pages 24)

Although Khwaja et al. and the present invention have the similar general objectives of resolving the quality control problem in botanical or herbal compositions, Khwaja et al. is markedly different from the present invention in at least two aspects: (1) the Khwaja method uses fractionation approach, while the present invention uses the whole batch of herbal extract; and (2) the Khwaja method involves testing the biological activity of each individual fraction of St. John's Wort, while the present invention involves determining the differential gene expression profile of the whole batch of herbal extract via a genomic-based bioassay.

More specifically, the Khwaja method comprises the steps of separating the St John's Wort composition into a plurality of marker fractions and determining the biological activity of each of the marker fractions of St John's Wort to provide a bioactivity fingerprint (col. 9, lines 9-14; col. 9, lines 24-30; col. 9, lines 56-62; and Fig. 6). In contrast, the present method includes, *inter alia*, determining the differential gene expression profile of a whole batch of a herbal composition to obtain an Herbal BioResponse Array for comparison.

Furthermore, inasmuch as it involves testing the biological activity of the fractions of St John's Wort, the Khwaja method is predicated on the association between St John's Wort and the diseases/indications that can be treated by St John's Wort. For example, Khwaja et al. state:

> The method of developing a PharmaPrint® for a botanical when a range of putative active components is known begins with a literature review. … For a given indication, the literature must be studied to confirm that the putative active components are actually associated with that disease state. In addition, if there are any bioassays known for the putative active components and known for the indication, the bioassays must be consistent with both the indication and the putative active components. (column 13, lines 22-49, underline added)

The method of developing a PharmaPrint® for a botanical when the putative active components are not known also begins with a literature review. It involves reviewing any chemical literature, biological literature, published bioassays or clinical data available for the botanical, or related botanicals, or for botanicals with related activities. Based on the disease state, a series of relevant bioassays is chosen. (column 17, lines 66-67 and column 18, lines 1-5, underline added)

That is, the biological activity tested in the Khwaja method is the biological effect of St John's Wort to certain diseases/indications. In contrast, the genomic-based bioassay used in the present method determines the differential gene expression profiles of the standardized and test batches for comparing their gene expression intensities and patterns. In other words, the present method is not predicated on the relationship between the herbal composition and any diseases or particular biological pathways.

In view of the foregoing, Khwaja et al. differs from the present method not only in the technical steps but also in the underlying principles.

Lockhart et al., an article in the field of gene expression molecular biology, discloses a method of monitoring the expression levels of a multiplicity of pre-selected genes. However, Lockhart et al. does not disclose or suggest determining the differential gene expression profiles and comparing their gene expression intensities and patterns, as claimed by the present method. Instead, Lockhart et al. suggests using the method for monitoring genes associated with certain biological specificities, such as specific diseases or biological pathways. For example, Lockhart et al. states:

> "Genes of particular interest for expression monitoring include genes involved in the pathways associated with various pathological conditions (e.g., cancer) and whose expression is thus indicative of the pathological condition." (column 4, line 64-67, underline added)

Thus, the combined disclosures of Khwaja et al. and Lockhart et al. do not teach or suggest the claimed limitations of the present method.

Furthermore, Applicants respectfully note that Dr. Dan Theodorescu states, on pages 4 and 5 of the Declaration under 37 C.F.R. 132 (executed on March 7, 2005 by Dr. Theodorescu and submitted on March 16, 2005 in the present application), that it is not customary for someone working in botanical products to be familiar with and/or scan the gene expression

molecular biology literature routinely. Dr. Theodorescu also states that the mindset and approach of workers in the botanical field for many years and certainly in the early nineties was very descriptive and non scientific, with scientific research and/or clinical trials of these products being rare. Therefore, one skilled in the art of quality control of botanical products, at the time of the present invention, would not combine the disclosures of Khwaja et al. and Lockhart et al., let alone modify the disclosed methods in such a particular manner to obtain the present invention.

Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of the outstanding rejection and early notice of allowance to that effect. Should the Examiner believe that a telephonic interview would expedite prosecution and allowance of this application, he is encouraged to contact the undersigned at his convenience.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No.50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

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Respectfully submitted,
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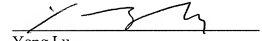
By: 

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